

SEQUENCE LISTING

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<120> GFR-alpha-1-RET Specific Agonists and Methods Therefor

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<170> PatentIn Ver. 2.0

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Tyr Ala Ser Glu Glu Lys Val Ile Phe Arg Tyr Cys Ala Gly Ser Cys
20 25 30

Pro Arg Gly Ala Arg Thr Gln His Gly Leu Ala Leu Ala Arg Leu Gln 35 40 45

Gly Gln Gly Arg Ala His Gly Gly Pro Cys Cys Arg Pro Thr Arg Tyr 50 55 60

Thr Asp Val Ala Phe Leu Asp Asp Arg His Arg Trp Gln Arg Leu Pro 65 70 75 80

Gln Leu Ser Ala Ala Ala Cys Gly Cys 85

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Cys Arg Leu Trp Ser Leu Thr Leu Pro Val Ala Glu Leu Gly Leu Gly 1 5 10 15

Tyr Ala Ser Glu Glu Lys Val Ile Phe Arg Tyr Cys Ala Gly Ser Cys 20 25 30

Pro Gln Glu Ala Arg Thr Gln His Ser Leu Val Leu Ala Arg Leu Arg 35 40 45

Gly Arg Gly Arg Ala His Gly Arg Pro Cys Cys Gln Pro Thr Ser Tyr 50 55 60

Ala Asp Val Thr Phe Leu Asp Asp Gln His His Trp Gln Gln Leu Pro 65 70 75 80

Gln Leu Ser Ala Ala Ala Cys Gly Cys 85

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Tyr Ala Ser Glu Glu Lys Ile Ile Phe Arg Tyr Cys Ala Gly Ser Cys
20 25 30

Pro Gln Glu Val Arg Thr Gln His Ser Leu Val Leu Ala Arg Leu Arg . 35 40 45

Gly Gln Gly Arg Ala His Gly Arg Pro Cys Cys Gln Pro Thr Ser Tyr
50 60

Ala Asp Val Thr Phe Leu Asp Asp His His His Trp Gln Gln Leu Pro 65 70 75 80

Gln Leu Ser Ala Ala Ala Cys Gly Cys 85

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Cys Val Leu Thr Ala Ile His Leu Asn Val Thr Asp Leu Gly Leu Gly 1 5 10 15

Tyr Glu Thr Lys Glu Glu Leu Ile Phe Arg Tyr Cys Ser Gly Ser Cys 20 25 30

Asp Ala Ala Glu Thr Thr Tyr Asp Lys Ile Leu Lys Asn Leu Ser Arg 35 40 45

Asn Arg Arg Leu Val Ser Asp Lys Val Gly Gln Ala Cys Cys Arg Pro
50 55 60

Ile Ala Phe Asp Asp Leu Ser Phe Leu Asp Asp Asn Leu Val Tyr 65 70 75 80

His Ile Leu Arg Lys His Ser Ala Lys Arg Cys Gly Cys 85 90

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<211> 93

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Cys Val Leu Thr Ala Ile His Leu Asn Val Thr Asp Leu Gly Leu Gly 1 5 10 15

Tyr Glu Thr Lys Glu Glu Leu Ile Phe Arg Tyr Cys Ser Gly Ser Cys
20 25 30

Glu Ser Ala Glu Thr Met Tyr Asp Lys Ile Leu Lys Asn Leu Ser Arg $35 \hspace{1cm} 40 \hspace{1cm} 45$

Ser Arg Arg Leu Thr Ser Asp Lys Val Gly Gln Ala Cys Cys Arg Pro
50 55 60

Val Ala Phe Asp Asp Asp Leu Ser Phe Leu Asp Asp Asn Leu Val Tyr 65 70 75 80

His Ile Leu Arg Lys His Ser Ala Lys Arg Cys Gly Cys 85 90

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Cys Val Leu Thr Ala Ile His Leu Asn Val Thr Asp Leu Gly Leu Gly 1 5 10 15

Tyr Glu Thr Lys Glu Glu Leu Ile Phe Arg Tyr Cys Ser Gly Ser Cys 20 25 30

Glu Ala Ala Glu Thr Met Tyr Asp Lys Ile Leu Lys Asn Leu Ser Arg 35 40 45

Ser Arg Arg Leu Thr Ser Asp Lys Val Gly Gln Ala Cys Cys Arg Pro 50 60

Val Ala Phe Asp Asp Asp Leu Ser Phe Leu Asp Asp Ser Leu Val Tyr 65 70 75 80

His Ile Leu Arg Lys His Ser Ala Lys Arg Cys Gly Cys 85 90

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Cys Gly Leu Arg Glu Leu Glu Val Arg Val Ser Glu Leu Gly Leu Gly 1 5 10 15

Tyr Ala Ser Asp Glu Thr Val Leu Phe Arg Tyr Cys Ala Gly Ala Cys 20 25 30

Glu Ala Ala Arg Val Tyr Asp Leu Gly Leu Arg Arg Leu Arg Gln 35 40 45

Arg Arg Arg Leu Arg Arg Glu Arg Val Arg Ala Gln Pro Cys Cys Arg 50 55 60

Pro Thr Ala Tyr Glu Asp Glu Val Ser Phe Leu Asp Ala His Ser Arg 65 70 75 80

Tyr His Thr Val His Glu Leu Ser Ala Arg Glu Cys Ala Cys 85 90

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Cys Gly Leu Arg Glu Leu Glu Val Arg Val Ser Glu Leu Gly Leu Gly 1 5 10 15

Tyr Thr Ser Asp Glu Thr Val Leu Phe Arg Tyr Cys Ala Gly Ala Cys 20 25 30

Glu Ala Ala Ile Arg Ile Tyr Asp Leu Gly Leu Arg Arg Leu Arg Gln 35 40 45

Arg Arg Arg Val Arg Arg Glu Arg Ala Arg Ala His Pro Cys Cys Arg
50 55 60

Pro Thr Ala Tyr Glu Asp Glu Val Ser Phe Leu Asp Val His Ser Arg 65 70 75 80

Tyr His Thr Leu Gln Glu Leu Ser Ala Arg Glu Cys Ala Cys 85 90

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His Arg Ser Asp Glu Leu Val Arg Phe Arg Phe Cys Ser Gly Ser Cys

Arg Arg Ala Arg Ser Pro His Asp Leu Ser Leu Ala Ser Leu Leu Gly 35 40 45

Ala Gly Ala Leu Arg Pro Pro Pro Gly Ser Arg Pro Val Ser Gln Pro 50 55 60

Cys Cys Arg Pro Thr Arg Tyr Glu Ala Val Ser Phe Met Asp Val Asn 65 70 75 80

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His Ser Ser Asp Glu Leu Ile Arg Phe Arg Phe Cys Ser Gly Ser Cys 20 25 30

Arg Arg Ala Arg Ser Gln His Asp Leu Ser Leu Ala Ser Leu Leu Gly 35 40 45

Ala Gly Ala Leu Arg Ser Pro Pro Gly Ser Arg Pro Ile Ser Gln Pro 50 55 60

Cys Cys Arg Pro Thr Arg Tyr Glu Ala Val Ser Phe Met Asp Val Asn 65 70 75 80

Ser Thr Trp Arg Thr Val Asp His Leu Ser Ala Thr Ala Cys Gly Cys 85 90 95

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Lys Gly Ser Cys Arg Leu Trp Ser Leu Thr Leu Pro Val Ala Glu Leu 20 25 30

Gly Leu Gly Tyr Ala Ser Glu Glu Lys Val Ile Phe Arg Tyr Cys Ala 35 40 45

Gly Ser Cys Pro Gln Glu Ala Arg Thr Gln His Ser Leu Val Leu Ala 50 55 60

Arg Leu Arg Gly Arg Gly Arg Ala His Gly Arg Pro Cys Cys Gln Pro 65 70 75 80

Thr Ala Phe Asp Asp Asp Val Thr Phe Leu Asp Asp Gln His His Tyr 85 90 95

His Ile Leu Arg Lys His Ser Ala Ala Ala Cys Gly Cys 100 105

<210> 12

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Cys Arg Leu Trp Ser Leu Thr Leu Pro Val Ala Glu Leu Gly Leu Gly 1 5 10 15

Tyr Ala Ser Glu Glu Lys Val Ile Phe Arg Tyr Cys Ala Gly Ser Cys 20 25 30

Pro Gln Glu Ala Arg Thr Gln His Ser Leu Val Leu Ala Arg Leu Arg 35 40 45

Gly Arg Gly Arg Ala His Gly Arg Pro Cys Cys Gln Pro Thr Ala Phe 50 55 60

Asp Asp Asp Val Thr Phe Leu Asp Asp Gln His His Tyr His Ile Leu 65 70 75 80

Arg Lys His Ser Ala Ala Ala Cys Gly Cys 85 90

<210> 13

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Ala Leu Ala His His His His His Asp Tyr Lys Asp Asp Asp 1 5 10 15

Lys Gly Ser Cys Arg Leu Trp Ser Leu Thr Leu Pro Val Ala Glu Leu 20 25 30

Gly Leu Gly Tyr Ala Ser Glu Glu Lys Val Ile Phe Arg Tyr Cys Ala 35 40 45

Gly Ser Cys Pro Gln Glu Ala Arg Thr Gln His Ser Leu Val Leu Ala 50 55 60

Arg Leu Arg Gly Arg Gly Arg Ala His Gly Arg Pro Cys Cys Gln Pro 65 70 75 80

Thr Ala Tyr Glu Asp Glu Val Thr Phe Leu Asp Asp Gln His His Tyr 85 90 95

His Thr Leu Gln Glu Leu Ser Ala Ala Cys Gly Cys 100 105

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Cys Arg Leu Trp Ser Leu Thr Leu Pro Val Ala Glu Leu Gly Leu Gly 1 5 10 15

Tyr Ala Ser Glu Glu Lys Val Ile Phe Arg Tyr Cys Ala Gly Ser Cys 20 25 30

Pro Gln Glu Ala Arg Thr Gln His Ser Leu Val Leu Ala Arg Leu Arg

35 40 45

Gly Arg Gly Arg Ala His Gly Arg Pro Cys Cys Gln Pro Thr Ala Tyr 50 55 60

Glu Asp Glu Val Thr Phe Leu Asp Asp Gln His His Tyr His Thr Leu 65 70 75 80

Gln Glu Leu Ser Ala Ala Ala Cys Gly Cys 85 90

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Ala Leu Ala His His His His His Asp Tyr Lys Asp Asp Asp 1 5 10 15

Lys Gly Ser Cys Arg Leu Trp Ser Leu Thr Leu Pro Val Ala Glu Leu 20 25 30

Gly Leu Gly Tyr Ala Ser Glu Glu Lys Val Ile Phe Arg Tyr Cys Ala 35 40 45

Gly Ser Cys Pro Gln Glu Ala Arg Thr Gln His Ser Leu Val Leu Ala 50 55 60

Arg Leu Arg Gly Arg Gly Arg Ala His Gly Arg Pro Cys Cys Gln Pro 65 70 75 80

Thr Arg Tyr Ġlu Ala Val Thr Phe Leu Asp Asp Gln His His Trp Arg 85 90 95

Thr Val Asp His Leu Ser Ala Ala Ala Cys Gly Cys 100 105

<210> 16

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Cys Arg Leu Trp Ser Leu Thr Leu Pro Val Ala Glu Leu Gly Leu Glý 1 5 10 15

Tyr Ala Ser Glu Glu Lys Val Ile Phe Arg Tyr Cys Ala Gly Ser Cys 20 25 30

Pro Gln Glu Ala Arg Thr Gln His Ser Leu Val Leu Ala Arg Leu Arg 35 40 45

Gly Arg Gly Arg Ala His Gly Arg Pro Cys Cys Gln Pro Thr Arg Tyr
50 55 60

Glu Ala Val Thr Phe Leu Asp Asp Gln His His Trp Arg Thr Val Asp 65 70 75 80

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His Leu Ser Ala Ala Ala Cys Gly Cys
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Tyr His Ile Leu Arg Lys His
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Tyr Ala Ser Glu Glu Lys Val Ile Phe Arg Tyr Cys Ala Gly Ser Cys 20 25 30

Pro Arg Gly Ala Arg Thr Gln His Gly Leu Ala Leu Ala Arg Leu Gln 35 40 45

Gly Gln Gly Arg Ala His Gly Gly Pro Cys Cys Arg Pro Thr Ala Phe 50 55 60

Asp Asp Asp Val Ala Phe Leu Asp Asp Arg His Arg Tyr His Ile Leu 65 70 75 80

Arg Lys His Ser Ala Ala Ala Cys Gly Cys 85 90

<210> 24

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Cys Gln Leu Trp Ser Leu Thr Leu Ser Val Ala Glu Leu Gly Leu Gly

Tyr Ala Ser Glu Glu Lys Val Ile Phe Arg Tyr Cys Ala Gly Ser Cys
20 25 30

Pro Arg Gly Ala Arg Thr Gln His Gly Leu Ala Leu Ala Arg Leu Gln 35 40 45

Gly Gln Gly Arg Ala His Gly Gly Pro Cys Cys Arg Pro Thr Ala Tyr
50 60

Glu Asp Glu Val Ala Phe Leu Asp Asp Arg His Arg Tyr His Thr Val 65 70 75 80

His Glu Leu Ser Ala Ala Ala Cys Gly Cys 85 90

<210> 25

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Cys Gln Leu Trp Ser Leu Thr Leu Ser Val Ala Glu Leu Gly Leu Gly

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Tyr Ala Ser Glu Glu Lys Val Ile Phe Arg Tyr Cys Ala Gly Ser Cys 20 25 30
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Pro Arg Gly Ala Arg Thr Gln His Gly Leu Ala Leu Ala Arg Leu Gln 35 40 45

Gly Gln Gly Arg Ala His Gly Gly Pro Cys Cys Arg Pro Thr Arg Tyr
50 55 60

Glu Ala Val Ala Phe Leu Asp Asp Arg His Arg Trp Arg Thr Val Asp 65 70 75 80

Arg Leu Ser Ala Ala Ala Cys Gly Cys 85

<210> 26

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Ala Leu Ser Gly Pro Cys Gln Leu Trp Ser Leu Thr Leu Ser Val Ala 1 5 . 10 15

Glu Leu Gly Leu Gly Tyr Ala Ser Glu Glu Lys Val Ile Phe Arg Tyr 20 25 30

Cys Ala Gly Ser Cys Pro Arg Gly Ala Arg Thr Gln His Gly Leu Ala 35 40 45

Leu Ala Arg Leu Gln Gly Gln Gly Arg Ala His Gly Gly Pro Cys Cys
50 55 60

Arg Pro Thr Ala Phe Asp Asp Asp Val Ala Phe Leu Asp Asp Arg His 65 70 75 80

Arg Tyr His Ile Leu Arg Lys His Ser Ala Ala Cys Gly Cys Gly 85 90 95

Gly

<210> 27

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Ala Leu Ser Gly Pro Cys Gln Leu Trp Ser Leu Thr Leu Ser Val Ala 1 5 15

Glu Leu Gly Leu Gly Tyr Ala Ser Glu Glu Lys Val Ile Phe Arg Tyr 20 25 30

Cys Ala Gly Ser Cys Pro Arg Gly Ala Arg Thr Gln His Gly Leu Ala 35 40 45

Leu Ala Arg Leu Gln Gly Gln Gly Arg Ala His Gly Gly Pro Cys Cys

50 55 60

Arg Pro Thr Ala Tyr Glu Asp Glu Val Ala Phe Leu Asp Asp Arg His 65 70 75 80

Arg Tyr His Thr Val His Glu Leu Ser Ala Ala Cys Gly Cys Gly 85 90 95

Gly

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<212> PRT

<213> Homo sapiens

<400> 28

Ala Leu Ser Gly Pro Cys Gln Leu Trp Ser Leu Thr Leu Ser Val Ala 1 5 10 15

Glu Leu Gly Leu Gly Tyr Ala Ser Glu Glu Lys Val Ile Phe Arg Tyr
20 25 30

Cys Ala Gly Ser Cys Pro Arg Gly Ala Arg Thr Gln His Gly Leu Ala 35 40 45

Leu Ala Arg Leu Gln Gly Gln Gly Arg Ala His Gly Gly Pro Cys Cys
50 60

Arg Pro Thr Arg Tyr Glu Ala Val Ala Phe Leu Asp Asp Arg His Arg 65 70 75 80

Trp Arg Thr Val Asp Arg Leu Ser Ala Ala Ala Cys Gly Cys Gly Gly 85 90 95

<210> 29

<211> 151

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<213> Homo sapiens

<400> 29

Arg Leu Lys Arg Ser Pro Asp His His His His His Asp Tyr Lys
5 10 15

Asp Asp Asp Lys Gln Ala Ala Leu Pro Arg Arg Glu Arg Asn 20 25 30

Arg Gln Ala Ala Ala Ser Pro Glu Asn Ser Arg Gly Lys Gly Arg
35 40 45

Arg Gly Gln Arg Gly Lys Asn Arg Gly Cys Val Leu Thr Ala Ile His 50 55 60

Leu Asn Val Thr Asp Leu Gly Leu Gly Tyr Glu Thr Lys Glu Glu Leu 65 70 75 80

Ile Phe Arg Tyr Cys Ser Gly Ser Cys Glu Ala Ala Glu Thr Met Tyr 85 90 95

Asp Lys Ile Leu Lys Asn Leu Ser Arg Ser Arg Arg Leu Thr Ser Asp 100 105 110

Lys Glu Gly Gln Ala Cys Cys Arg Pro Val Ala Phe Asp Asp Asp Leu 115 120 125

Ser Phe Leu Asp Asp Ser Leu Val Tyr His Ile Leu Arg Lys His Ser 130 135 140

Ala Lys Arg Cys Gly Cys Ile 145 150

<210> 30

<211> 114

<212> PRT

<213> Homo sapiens

<400> 30

Arg Leu Pro Arg Ala Leu Ala His His His His His Asp Tyr Lys 5 10 15

Asp Asp Asp Lys Gly Ser Cys Arg Leu Trp Ser Leu Thr Leu Pro
20 25 30

Val Ala Glu Leu Gly Leu Gly Tyr Ala Ser Glu Glu Lys Val Ile Phe 35 40 45

Arg Tyr Cys Ala Gly Ser Cys Pro Gln Glu Ala Arg Thr Gln His Ser 50 55 60

Leu Val Leu Ala Arg Leu Arg Gly Arg Gly Arg Ala His Gly Arg Pro 65 70 75 80

Cys Cys Gln Pro Thr Ser Tyr Ala Asp Val Thr Phe Leu Asp Asp Gln 85 90 95

His His Trp Gln Gln Leu Pro Gln Leu Ser Ala Ala Ala Cys Gly Cys 100 105 110

Gly Gly

<210> 31

<211> 118

<212> PRT

<213> Homo sapiens

<400> 31

Arg Ala Arg Arg Pro Gly Ala His His His His His Asp Tyr Lys
5 10 15

Asp Asp Asp Lys Arg Gly Cys Val Leu Thr Ala Ile His Leu Asn 20 25 30

Val Thr Asp Leu Gly Leu Gly Tyr Glu Thr Lys Glu Glu Leu Ile Phe 35 40 45

Arg Tyr Cys Ser Gly Ser Cys Glu Ala Ala Glu Thr Met Tyr Asp Lys 50 55 60

Ile Leu Lys Asn Leu Ser Arg Ser Arg Arg Leu Thr Ser Asp Lys Val 65 70 75 80

Gly Gln Ala Cys Cys Arg Pro Val Ala Phe Asp Asp Asp Leu Ser 85 90 95

Phe Leu Asp Asp Ser Leu Val Tyr His Ile Leu Arg Lys His Ser Ala 100 105 110

Lys Arg Cys Gly Cys Ile 115

<210> 32

<211> 25

<212> PRT

<213> Homo sapiens

<400> 32

Arg Arg Ala Arg Pro Gly Ala His His His His His His Asp Tyr Lys $5 \hspace{1cm} 10 \hspace{1cm} 15$

Asp Asp Asp Lys Arg Gly Cys Arg 20 25